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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/778,200	02/06/2001	John Kisiday	01997/537001	8784

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EXAMINER	
NAFF, DAVID M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 09/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/778,200	KISIDAY ET AL.	
	Examiner	Art Unit	
	David M. Naff	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,19,20,22-24 and 27-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,19,20,22-24 and 27-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/26/06 has been entered.

An amendment of 6/26/06 in response to an office action of 6/22/05 amended claims 1, 30 and 36-39.

It is noted the amendment labels claims 33-35 as new. However, these claims are previously presented. Additionally, claim 21 has been labeled as cancelled, and the complete claim thereafter recited. The claim should be indicated as cancelled by merely reciting "cancelled" after the claim number as done when canceling claims 25 and 26.

Claims examined on the merits are 1-8, 19, 20, 22-24 and 27-40, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-8, 19, 20, 22-24 and 27-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are confusing by claim 1 requiring the scaffold formed by the peptides self-assembling to encapsulate cells, and the claim in line 1 requiring the scaffold to comprise only the peptides. If cells are encapsulated, the scaffold will comprise the cells in addition to the peptides. Claim 1 should be amended in line 1 by inserting --- and living cells --- after "peptides", and in line 4 by inserting --- the --- before "living".

Claim Rejections - 35 USC § 103

Claims 1-3, 5-8, 19, 22-24, 27-29, 31, 32, 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holmes et al (5,955,343) in view of Hubbell (6,129,761) for reasons in the previous office action of 6/22/05, and for reasons herein.

The claims are drawn to a macroscopic scaffold containing amphiphilic peptides having alternating hydrophobic and hydrophilic amino acids, which are complementary and structurally compatible and self-assemble into a beta-sheet macroscopic scaffold, and the scaffold is formed by the peptides self-assembling to encapsulate living cells to provide a three-dimensional arrangement of the cells within the scaffold.

Holmes et al (col 11, lines 32-35) disclose culturing cells on a membrane or matrix formed by self-assembling of peptides. The peptides are stable in aqueous solution and self-assemble into a macroscopic structure or matrix when exposed to salt (col 1, lines 32-35). The structures produced can also encapsulate cells since the pore size of the structure is large enough to allow nutrients and

products to diffuse, and cells being larger than the pores are contained (col 12, lines 4-9).

Hubbell discloses a scaffold for implanting containing cells encapsulated in a hydrogel (col 5, lines 55-60), and which can contain biologically active agents such as therapeutic agents (col 7, lines 15-21). The hydrogel is produced by forming a polymer solution containing cells, and cross-linking the polymer.

Rather than culture the cells on the membrane or matrix of Holmes et al, it would have been obvious to encapsulate the cells in the membrane or matrix as suggested by Hubbell encapsulating cells in a hydrogel for implanting and by Holmes et al disclosing encapsulating cells in the membrane or matrix as an alternative to attaching cells to the membrane or matrix. The membrane or matrix of Holmes et al is inherently a scaffold. The peptides of Holmes et al may be combined with collagen (col 11, lines 26-28), which is an extracellular matrix protein. Chondrocytes disclosed by Hubbell (col 11, line 58) produce extracellular matrix protein as required by claims 6 and 7, and it would have been obvious to use chondrocytes to produce the collagen disclosed by Holmes et al. The collagen would have inherently resulted in an increase in strength, stiffness and equilibrium compression modulus as required by dependent claims 22-24. Growth factors as disclosed by Holmes et al (col 11, lines 35-38) would be a chemoattractant as in claim 2. Additionally, the membrane or matrix of Holmes et al may contain a therapeutic compound (col 11, lines 3-11) as in claim 2. The condition of claim 8 will be inherent when

encapsulating cells in the membrane or matrix of Holmes et al. Hubbell discloses molding (col 12, line 22) and would have suggested pre-shaping as in claim 29. Selecting an optimum amount of cells as in claim 31 for a particular function would have been within the skill of the art. Cells encapsulated in the membrane or matrix of Holmes et al will inherently divide as in claim 32 after being placed in a culture medium as suggested by Holmes et al (col 12, lines 1-9). Peptides used by Holmes et al inherently have an adhesion site as in claim 3. The conditions of claims 34 and 35 will be inherent when encapsulating cells in the membrane or matrix of Holmes et al as set forth above.

Response to Arguments

The response urges that Holmes et al (column 12, lines 1-9) layer cells between membranes. However, column 12, lines 1-9, does not disclose layering cells between membranes, but instead discloses stacking membranes containing cells. The cells being larger than membrane pore size does not prevent cells being in the membrane as urged by in the response since the cells can be combined with the peptides before they self-assemble to form the membrane. Contrary to the argument in the response, Holmes et al (col 12, lines 4-9) clearly suggest encapsulating cells in the membrane, and not forming a cell layer between membrane layers.

The response urges that Holmes et al do not describe how to encapsulate cells in the membrane. However, how to encapsulate the cells will be obvious to one of ordinary skill in the art when Hubbell

is also considered, and suggesting that cells can be encapsulated simply by adding cells to the peptides before self-assembly and allow self-assembly to occur in the presence of the cells. Self-assembly of the peptides of Holmes et al does not occur until after a salt is added. Obviously, cells can be combined with the peptides before the salt is added so that self-assembly will occur in the presence of the cells and result in entrapment of the cells in the membrane or matrix. This will be further apparent from Hubbell cross-linking a polymer in presence of cells to encapsulate the cells in a cross-linked polymer. Incubating cells and peptides under conditions that do not allow self-assembly, and then adding an electrolyte to cause the peptides to self-assemble would have been obvious from Holmes et al disclosing that the peptides do not self-assemble in aqueous solution until a salt is added. This procedure would have been an obvious method to use when encapsulating cells as suggested by Holmes et al (col 12, lines 5-10), and is also suggested by Hubbell disclosing mixing cells with a polymer solution and then cross-linking the polymer to form a hydrogel. Holmes et al believed that encapsulated cells in the self-assembled peptide matrix can survive, or otherwise encapsulating cells would not have been mentioned. There is nothing to suggest that self-assembly of peptides while cells are present will cause cells not to survive, or will prevent the peptides from self-assembling. Cells surviving cross-linking of a polymer to form a hydrogel as disclosed by Hubbell would have led one to expect that cells can also survive self-assembly of peptides. The structure of a matrix formed by self-

assembly of peptides is not sufficiently different from a matrix formed by cross-linking a polymer to lead one to believe that cells cannot survive in the self-assembled peptide matrix.

Applicants urge that Hubbell is not self-assembling peptides to encapsulate cells. However, Hubbell is not applied alone, but is combined with Holmes et al suggesting that cells can be encapsulated in a membrane resulting from self-assembling of peptides (col 12, lines 5-9).

Claim Rejections - 35 USC § 103

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-3, 5-8, 19, 22-24, 27-29, 31, 32, 34 and 35 above, and further in view of Holmes et al (PNAS).

The claim requires cells encapsulated to be neurons.

Holmes et al (PNAS) disclose attaching neurons to a self-assembling peptide scaffold and growing the neurons. The peptides self-assemble to form a hydrogel (first page, left col, about line 8)

When encapsulating cells in a self-assembling peptide membrane or matrix as suggested by Holmes et al and Hubbell as set forth above, it would have been obvious to use neurons as the cells to obtain the function of neurons as suggested by Holmes et al (PNAS) when attaching neurons to a self-assembling peptide scaffold.

Response to Arguments

The response relies on arguments traversing the above rejection to traverse this rejection. These arguments are unpersuasive for reasons set forth above.

Claim Rejections - 35 USC § 103

Claims 30, 33 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-3, 5-8, 19, 22-24, 27-29, 31, 32, 34 and 35 above, and further in view of Lee et al (6,306,169 B1).

The claims require subjecting the scaffold to static or dynamic compression or a combination thereof.

Lee et al disclose (col 8, lines 31-44) subjecting cells in a construct prior to implantation to mechanical loading in a static or dynamic manner that can be in the form of uniaxial compression. Dynamic frequencies can range from 0.001-10 Hz, preferably 0.1-3 Hz. Advantages of applying mechanical strain include increasing metabolic parameters known to influence the success of tissue engineering repair, and producing oriented cell proliferation that is a feature of articular cartilage (col 8, lines 45-64).

When encapsulating cells in a self-assembling peptide membrane or matrix as suggested by Holmes et al and Hubbell as set forth above, it would have been obvious subject the cells in the membrane or matrix to static or dynamic compression for advantages suggested by Lee et al when subjecting cells in a construct to mechanical loading that can be in the form of static or dynamic compression.

Claim Rejections - 35 USC § 103

Claims 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-3, 5-8, 19, 22-24, 27-29, 31, 32, 34 and 35 above, and further in view of Seifert

(5,175,093) and Krzyzek et al (5,472,869), and if necessary in further view of Chenite et al (6,344,488 B1).

The claims require preparing the scaffold by a method of incubating the peptides and cells in an aqueous solution comprising a predetermined concentration of a carbohydrate or glycerol to provide sufficient osmolarity to maintain cell viability and under conditions that do not allow the peptides to substantially self-assemble, and adding an electrolyte that initiates the peptides to self-assemble into a beta-sheet macroscopic scaffold and encapsulate the cells in the scaffold. The solution containing the peptides and cells prior to adding the electrolyte may be in a pre-shaped mold to determine volume or shape of the scaffold. The cells can be first incubated in the solution providing osmolarity, followed by adding the peptides and the electrolyte.

Seifert discloses controlling osmolarity when immobilizing cells in alginate beads to provide an environment for viability. The osmolarity can be controlled with polyethylene glycol or by adding an osmoticum (col 7, lines 1-12).

Krzyzek et al disclose using an osmoticum to preserve cell viability (col 4, lines 46-53, and col 12, lines 13-20). The osmoticum can be glycerol (col 12, line 16, and col 20, line 64).

Chenite et al disclose maintaining osmolarity for viability of cells when forming a gel containing cells.

When encapsulating cells in a self-assembling peptide membrane or matrix as suggested by Holmes et al and Hubbell as set forth above, it

would have been obvious combine the cells with glycerol as an osmoticum prior to self-assembly of the peptides to form the membrane or matrix to maintain an environment for cell viability as suggested by Seifert using an osmoticum for viability when immobilizing cells and by Krzyzek et al using glycerol as an osmoticum to maintain cell viability. If needed, Chenite et al would have further suggested controlling osmolarity to maintain cell viability.

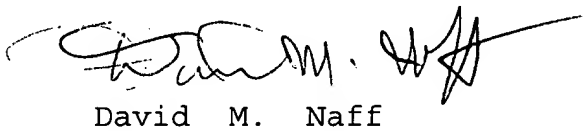
Conclusion

Claim 20 is free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David M. Naff
Primary Examiner
Art Unit 1651

DMN
8/31/06